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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/571,469	03/13/2006	Frank Mattner	286808US0PCT	6417

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EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/571,469	MATTNER ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 7 April 2010 have been entered. Claims 5-11 are pending and under examination.

Maintained Rejections

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5-8 and 10-11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over DeMattos 2001 (Proc Natl Acad Sci USA 98:8850-8855) in view of Kojima 2001 (J. Biochem. Biophys. Methods 49:241-251).

This rejection stands for the reasons previously made of record and explained in further detail here. The teachings of DeMattos and of Koijma have been set forth previously and therefore will be summarized rather than reiterated in their entirety. Briefly, Demattos teaches that peripheral administration of a monoclonal antibody against Aβ, called m266, leads to a 1000-fold increase in the amount of Aβ in the bloodstream and a decrease in the amount of this toxic protein in the brains of mice. DeMattos indicates that the most likely mechanism is that the antibody alters the equilibrium of Aβ between brain and plasma, and as Aβ is sequestered in periphery once it is bound to the circulating antibody, the balance of Aβ between the blood and the brain is changed. In order to compensate for the decreased Aβ in the blood, Aβ exits the

brain and enters the bloodstream, explaining the large increase in circulating Aβ observed. The m266 antibody used binds to an epitope within residues 13-28 of Aβ (DeMattos, p. 8851, first paragraph of the Results and Discussion section), so it will bind to both Aβ40 and Aβ42, as recited in claims 6 - 8. The PDAPP mice can be construed as both suffering from AD as recited in claim 10 and at risk of AD as recited in claim 11. DeMattos suggests that antibodies against Aβ can be used to drawn Aβ out of the brain and clear it from the patient, which would be therapeutic in patients with AD; see p. 8854 last paragraph. However DeMattos while teaches peripheral administration of the antibody and suggests using antibodies against Aβ to remove this protein from the brain and into the blood, the reference does not explicitly teach contacting the blood or plasma flow of a patient with an apheresis device that has the anti-Aβ antibodies attached to the surface of a solid carrier as recited in claim 5.

Kojima teaches treatment of amyloid diseases by extracorporeal apheresis of plasma over an immunoaffinity membrane. Specifically, Kojima teaches that antibodies against either β2-macroglobulin or serum amyloid P can be immobilized on a membrane, and that when the plasma from a subject is passed through an apheresis device containing such a membrane, a large percentage of the relevant protein is removed from the serum. Additionally at p. 247 first complete paragraph Kojima teaches anti-SAP antibody can remove over 90% of this protein from plasma. The reference therefore teaches one of ordinary skill in the art how to prepare an apheresis apparatus comprising antibodies against amyloid-inducing polypeptides immobilized on a solid surface, and teaches one of ordinary skill how to use such an apparatus to remove these amyloid-causing proteins from the bloodstream of a patient susceptible to disease. However Kojima does not teach methods of treating Alzheimer's disease or using antibodies against Aβ.

Nevertheless, it would have been obvious to one of ordinary skill in the art to modify the teachings of DeMattos, by using an antibody-based apheresis system as taught by Kojima, thereby arriving at the invention encompassed by claims 5-8 and 10-11. Doing so would have been obvious, since DeMattos teaches that contacting blood with antibodies against Aβ is therapeutic for Alzheimer's disease, and that the antibodies need not reach the brain to have their effect (see for example DeMattos, p. 8850 paragraph spanning the two columns and p. 8854 second column first complete paragraph). It would be reasonable to expect success, as Kojima demonstrates that the method of using an apheresis device with antibodies is effective to remove circulating amyloid proteins, so one of ordinary skill would have reasonably expected

that other amyloid proteins could be removed by the same technology, particularly in light of DeMattos's teaching that peripheral administration of the antibody is therapeutic, and that the antibody need not enter the brain in order to have its effect.

Applicant traversed the examiner's determination of obviousness on several grounds, each of which will be answered in turn. According to applicant, the invention as claimed would not have been obvious over DeMattos in view of Kojima for the following reasons:

A) Kojima does not disclose that amyloid deposition decreases after apheresis,

B) The differences between DeMattos's teachings and those of Kojima are so great that there would not be a motivation to combine them (remarks paragraph spanning pp. 4-5), and

C) The examiner has mischaracterized the in vitro findings of DeMattos, and the findings do not support a conclusion of obviousness.

Applicant's arguments have been fully considered but they are not persuasive. With respect to A), the examiner concedes the reference by Kojima does not explicitly teach that amyloid deposition is decreased with extracorporeal apheresis. However, the reference by DeMattos teaches that administering the m266 antibody decreases amyloid plaque formation in the brains of mice (see abstract) and suggests that similar effects will be seen in human Alzheimer's patients. Thus while the reference by Kojima does not indicate that an anti-amyloid protein antibody will decrease plaque formation, the DeMattos reference cures this alleged deficiency. The DeMattos reference differs from the claimed invention only in that the latter requires use of an apheresis device, whereas the former teaches peripheral administration. Kojima was relied upon by the examiner to show that this small difference was known and would have been obvious to one of ordinary skill in that art, in that apheresis devices comprising antibodies against amyloid proteins were known and would reasonably be expected to remove amyloid β protein from the blood. Given that DeMattos teaches that sequestration of the Aβ protein by the antibody in the periphery leads to more APP-containing Aβ leaving the brain, an artisan of ordinary skill would have a reasonable expectation of success in modifying DeMattos's method by using an apheresis device such as that described by Kojima.

With respect to B) the examiner respectfully disagrees that the teachings of the two references are so far apart that there would have been no way to understand that the methods of Kojima could be applied to the techniques of DeMattos. Each of the references is on point to treating medical conditions caused by amyloid-inducing proteins by using antibodies that bind to

the proteins. The apheresis device discussed in Kojima could easily be adapted to hold an anti-Aβ antibody rather than an anti-β2 macroglobulin antibody.

With respect to C), the examiner concedes that the in vitro system characterized by DeMattos is not a perfect model of an apheresis system. However, the point of the in vitro experiments set forth by DeMattos (depicted in Figure 1) is to show that the ability of m266 antibody to bring Aβ across a semi-permeable membrane (i.e., a model of a physiological membrane) is specific to this antibody and is not seen with antisera (IgG) generally, or with non-specific proteins (BSA), or even other Aβ-binding proteins (ApoE4). The data presented by DeMattos indicate that the ability to bring Aβ across the membrane is unique to this antibody. Given that it can pull Aβ out of the brain, using m266 antibody in an apheresis device rather than administering it is only a small difference which does not represent a patentable contribution over the prior art.

For at least the reasons above, the rejection under 35 USC 103(a) is maintained.

3. Claims 5-11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over DeMattos in view of Kojima as applied to claims 5-8 and 10-11 above, and further in view of Boos (U.S. Patent 5,679,775, issued 21 October 1997).

The reasons why claims 5 - 8 and 10 - 11 are obvious over DeMattos in view of Kojima are set forth above. While Kojima teaches a column within an apheresis device, which is suitable for removing Aβ from biological fluids, the reference does not explicitly teach a sterile pyrogen-free column as recited in claim 9.

Boos teaches sterile pyrogen-free columns for apheresis. See Example 1 spanning columns 6 - 7. The reference teaches that the columns can be used to remove disease related proteins from human blood or plasma; see column 6 lines 17 - 42. However Boos does not teach sterile pyrogen-free apheresis devices comprising antibodies that bind Aβ or APP.

It would have been obvious to one of ordinary skill in the art to use sterile pyrogen-free columns as taught by Boos in the methods rendered obvious by DeMattos in view of Kojima, thereby arriving at the invention of claim 9. The motivation to do so would be to use a device that would be less likely to infect patients, as sterile pyrogen-free materials would pose less of a risk of infection.

Applicant did not traverse the examiner's determination that the specific limitations of claim 9, namely a sterile pyrogen-free column, would have been obvious to one of ordinary skill

in the art in view of the teachings of Boos. Rather applicant argued that the other two references (DeMattos and Kojima) do not render obvious the claimed invention, and that Boos does not cure an alleged deficiency. For the reasons set forth in the rejection above, DeMattos and Kojima, taken together, render obvious the claimed methods. This rejection, which includes claim 9, is maintained as the reference by Boos teaches and renders obvious a sterile and pyrogen-free column.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5 - 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22 – 27 of copending Application No. 11/571970. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the '970 application are specific as they require an

additional step (administration of an agent) beyond the step of apheresis as claimed herein. The instant claims are generic, as they require only the step of using the apheresis device, which also appears in independent claim 22 of the '970 application. As the claims in the '970 application are species, they would anticipate the instant claims 5 - 11. Note that at p. 11 of the specification of the '970 application, anti-Aβ antibodies are indicated to be preferred components of the apheresis device, and that sterile pyrogen-free columns are preferred.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant did not traverse the examiner's rejection for obviousness-type double-patenting, but requested withdrawal of the rejection assuming the claims were otherwise allowable. As set forth above, the claims are not allowable, so this rejection stands.

Conclusion

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
May 13, 2010